

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A01N 37/16 // (A01N 37/16, 25:30)		A1	(11) International Publication Number: WO 94/14321 (43) International Publication Date: 7 July 1994 (07.07.94)
(21) International Application Number: PCT/GB93/02520 (22) International Filing Date: 9 December 1993 (09.12.93) (30) Priority Data: 9227020.6 24 December 1992 (24.12.92) GB		(81) Designated States: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>	
(71) Applicant (for all designated States except US): SOLVAY INTEROX LIMITED [GB/GB]; Baronet Works, Baronet Road, Warrington, Cheshire WA4 6HB (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): FRENCH, Madeline, Susan [GB/GB]; 12 Delphfield, Norton Cross, Runcom WA7 6RW (GB). HARVEY, Anita, Jane [GB/GB]; 87 Dove Close, Birchwood, Warrington WA3 6QH (GB). (74) Agent: PEARCE, Timothy; Solvay Interox Limited, Patent Department, P.O. Box 51, Moorfield Road, Widnes WA8 0FE (GB).			
(54) Title: MICROBICIDAL COMPOSITIONS			
(57) Abstract			
<p>Microbicidal compositions having activity over a broad pH range are provided. The compositions comprise a peracid and a nonionic surfactant according to the general chemical formula: $R-(OCH_2CH_2)_n-(OCH_2CH_2CH_3)_p-O-R'$, wherein R represents an alkyl group of at least 6 carbon atoms, n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms. The compositions can additionally comprise a cationic surfactant.</p>			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Larvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

Microbical Compositions

The present invention concerns microbical compositions. More specifically, the present invention concerns peracid microbical compositions, and still more specifically, peracid microbical peracid compositions having 15 activity over a broad pH range.

The use of aliphatic peracids as microbicides is well known in the art. Such solutions have found favour because they offer a microbical system which has reduced environmental impact and are completely biodegradable. It has also long been recognised that the microbical activity of aliphatic peracids is 20 strongly dependant on the pH at which the peracid is employed, and that the activity decreases as the pH increases. This is particularly evident as the pH of the peracid solution approaches neutral pH. Accordingly, the most effective use of aliphatic peracid microbicides has hitherto occurred at acidic pH. A number of systems require disinfection at alkaline pH or exist in their natural 25 state at alkaline pH, and are thus not well suited to disinfection by such peracid-based microbicides. It remains an ongoing desideratum to identify peracid-based microbicide compositions having activity over a broader and/or higher pH range.

It is an object of certain aspects of the present invention to provide 30 aliphatic peracid microbicide compositions having improved activity over a broader and/or higher pH range.

It is a further object of some or other aspects of the present invention to provide microbical compositions having improved activity against gram-negative bacteria over a broader and/or higher pH range.

35 According to the present invention, there are provided peracid compositions having microbical activity over a broad pH range, characterised in that they

comprise an effective amount of a peracid and a nonionic surfactant according to the general chemical formula (1):



wherein R represents an alkyl group of at least 6 carbon atoms n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms.

According to a second aspect of the present invention, there is provided a microbicidal process employing as microbicide an effective amount of a peracid and a nonionic surfactant, characterised in that the nonionic surfactant has the general formula: $R-(OCH_2CH_2)_n-(OCH_2CH_2CH_3)_p-O-R'$

wherein R represents an alkyl group of at least 6 carbon atoms n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms.

By employing the selected alkoxylated alcohol surfactant of formula (1), it has been found that the effectiveness of peracid microbicides is enhanced at treatment pHs of above pH 6, i.e. in approximately neutral or mildly alkaline pH conditions, thereby extending advantageously the effective treatment range for the peracids.

In formula (1), R often contains from about 6 to about 18 carbons, and especially from about 8 to about 12 carbons and in many instances comprises a linear group. R can be synthetically derived, or can be obtained from natural sources, for example, from tallow. R' in formula (1) often contains from 2 to 4 carbon atoms and typically comprises 3 carbon atoms. The weight proportion of alkoxylate i.e. ethoxylate or the total of ethoxylate and propoxylate in the surfactant is often selected in the region of about 55% to about 90%; n + p in formula (1) in many instances totalling from 4 to 20.

It will be recognised that compositions according to the present invention can be supplied in a number of different forms or can be produced immediately prior to use depending, for example, on the particular composition desired, or on the particular application. For instance, in certain embodiments of the present invention, the composition is in the form of a ready-to-use solution which can be used without requiring dilution. In certain other embodiments, the composition is in the form of a concentrated solution which may be employed without dilution, but is primarily intended for dilution prior to use. In further embodiments, the components are provided as a two pack system, with the first solution comprising aqueous peracid solution and optionally a fraction of the nonionic surfactant, and the second solution comprising the remaining

fraction of the nonionic surfactant. In these two pack systems, the second solution can be used to dilute the first solution to produce a composition ready for immediate use, or a composition which can be diluted further prior to use.

The weight of alkoxylated alcohol in the invention compositions can be 5 selected within a wide range. In many embodiments, where the compositions are ready for use or supplied as a concentrate, it is at least 0.1% w/w and often is not greater than about 50% w/w. Advantageous results have been obtained for ready to use solutions at a concentration chosen in the range of about 4 to about 15% w/w of the alkoxylated alcohol. Where a concentrate is 10 diluted prior to use, the concentration of alcohol ethoxylate in the in use solution is often in the range of from about 0.1% w/w to about 15% w/w.

Where the components are provided as a two pack system, the second solution can contain up to 100% of nonionic surfactant, however, in many embodiments, the nonionic surfactant will be present at from about 20% w/w 15 to about 80% w/w. When nonionic surfactant is employed in the first solution in a two pack system, the concentration of the nonionic surfactant is typically in the range of from about 4 to about 25% w/w.

The peracid can comprise any percarboxylic acid, particularly water-soluble percarboxylic acids and especially is selected from low or medium molecular 20 weight aliphatic percarboxylic acids such as those containing up to 9 carbons. The invention will be described with particular reference to peracetic acid, but for example, perpropionic acid may be employed instead of or together with peracetic acid.

The concentration of peracid in preformed compositions intended for 25 storage and/or transportation can be selected over a wide range, such as from about 0.01% to 40% w/w. In many embodiments, the compositions comprise a dilute solution of the peracid, such as from about 0.5% to about 10% w/w. The actual selection of the peracid is often a matter at the discretion of the producer, for his own convenience, balancing the beneficial and 30 disadvantageous effects of a chosen concentration. Concentrations of around 2 to 3% w/w peracid and from about 4 to about 5.5% w/w peracid are quite popular as compromises that are readily transportable without transporting too much water.

In many desirable compositions according to the present invention, which 35 are intended for storage and or transportation, the peracid is made by a reaction between the corresponding carboxylic acid or carboxylic acid anhydride and hydrogen peroxide in an aqueous medium. It is particularly

desirable to employ compositions in which the peracid is present at a concentration that is substantially in equilibrium with residual concentrations of its corresponding carboxylic acid and hydrogen peroxide. In such compositions, the concentration of hydrogen peroxide is often selected in the 5 range of from about 0.1 to 30% w/w and the concentration of carboxylic acid from about 0.5 to about 50% w/w. In practice, the weight ratio of carboxylic acid e.g. acetic acid or hydrogen peroxide relative to the peracid can be varied at the discretion of the producer/user within the entire range, provided that an appropriate concentration of the other reagent is present. In general terms, for 10 a stable equilibrium, a low peroxide concentration is balanced by a high carboxylic acid concentration, and vice versa, and ratio of peroxide plus carboxylic acid to peracid increases as the concentration of peracid decreases. For many dilute, transportable peracid compositions containing less than 6% peracid, the weight ratio of peroxide to peracid and of carboxylic acid to 15 peracid are each often selected in the range of from about 1:10 to about 10:1.

The transportable compositions can be employed neat, for example in the disinfection of hard surfaces such as work surfaces, equipment or sanitary ware, particularly if they contain less than 6% peracid, but they are often diluted with water before use or it is an aqueous medium which it is intended 20 to disinfect. The extent of dilution is at the discretion of the user, taking into account the extent and nature of the infecting micro-organisms which it is desired to kill, the period available for the kill and the operational conditions such as the temperature. Where the disinfection process involves a manual treatment stage, for example, distributing a composition over a hard surface 25 with a cloth, it is often desirable that the peracid concentration in the solution in use is less than about 0.1%.

It is convenient to express the concentration of the disinfectant composition by reference to the concentration of the peracid. The alkoxylated alcohol is present at a relative concentration thereto as indicated previously 30 herein. The peracid concentration is usually at least 5 mg/l and often up to 1000 mg/l. For a number of micro-organisms, a concentration of between 25 and 400 mg/l is selected. Depending on the conditions, though, for shock treatments, peracid concentration of above 1000 mg/l, for example up to about 10000 mg/l can be contemplated and for prolonged contact, a concentration of 35 1 to 5 mg/l peracid can sometimes be appropriate.

It will be recognised that the advantage of the invention composition, compared with prior disclosed compositions not containing the alkoxylated

alcohol, is that it is relatively more effective at approximately neutral or mildly alkaline compositions, and especially at a pH of from above 6 to 8. The user can obtain the benefit of a similar extent of disinfection using a peracid composition, such as peracetic acid at a higher pH, i.e. avoiding or reducing the 5 extent of pH adjustment, or alternatively he can obtain improved disinfection if he chooses not to acidify.

In theory, microbicidal compositions can contain other active microbicides in order to augment the activity from peracids, but there can be no guarantee that the addition of further components will improve the overall microbicidal 10 effectiveness. Some combinations of peracid with other components are unstable and others show little or no detectable change in performance, at least with reference to various widespread target micro-organisms.

One such class of other microbicides comprises quaternary ammonium compounds, a class of cationic surfactants. They are widely available, and 15 hence are attractive, but there can be difficulties associated with their use.

Within the spectrum of micro-organisms that it is desired to control, i.e. kill or inactivate, by the application of a microbicidal composition are bacteria.

Bacteria themselves are generally divided into two classes, gram-negative and gram-positive bacteria. It is generally recognised that, of the two classes, 20 gram-positive bacteria are, in many cases, relatively easy to control by the application of quaternary ammonium compounds, but that gram negative bacteria are much more resistant to them. It is particularly desirable to control gram negative bacteria, because the group comprises many well known pathogens, for example, many species of faecal bacteria, pseudomonads which 25 can cause skin irritation, and other species of bacteria, such as salmonella which can cause food poisoning. Self-evidently, it would be advantageous to identify microbicidal compositions having improved activity against gram negative bacteria.

It has been found to be especially desirable to employ the combination of 30 peracid and alkoxylated alcohol in conjunction with a quaternary ammonium cationic surfactant, since by so doing, the resultant three component combination has been shown to be particularly effective against Gram negative bacteria. The quaternary ammonium compound, which can be represented by the general formula $R^aR^bR^cR^dN^+ Q^-$ in which substituents R^a , R^b , R^c , and R^d 35 each represent an alkyl or aryl group or two of which combine with the nitrogen to form a heterocyclic nucleus, the total number of carbons in R^a to R^d normally comprising from about 10 to about 30 carbons. One or two of

the substituents normally contains from 8 to 18 linear carbons often from C12 to C16, or forms part of the heterocyclic nucleus such pyridinium. One of the substituents can conveniently comprise a benzyl group. The remaining substituents usually are selected from C1 to C4 alkyl groups, and especially 5 methyl or ethyl. Q represents a counterion such as hydroxyl, sulphate or alkyl sulphate.

The quaternary ammonium cationic surfactant (QACS) is often incorporated at a relatively small proportion of the overall composition, such as up to about 5% w/w in a dilutable composition, or up to about 0.5% w/w in a composition 10 ready for use without further dilution. It will be recognised that in a two pack system, the QACS can be incorporated in either or both of the solutions at a concentration selected accordingly.

A particularly effective range of compositions comprises peracetic acid at a weight concentration in the region of about 2.0 to 5.5%, preferably in the 15 presence of sufficient hydrogen peroxide and acetic acid selected together in the ranges of 1 to 20% and 1 to 50% respectively to obtain an equilibrium composition, from 4 to 15% alkoxylated alcohol and from 0.05 to 0.5% QACS. Such compositions may often be diluted by a factor in the range of from about 10 to about 1000, depending on the peracid concentration before dilution and 20 its desired concentration for disinfection.

The invention compositions are particularly intended for use in the food, beverage and allied industries. The beverage industries include brewing, wine-making and alcohol distillation, and in dairies. In such industries, it is especially important to guard against the contamination of food and drink 25 intended not only for human consumption, but also that intended for consumption by livestock, and pets. In such industries, the compositions can be used to disinfect brewing vessels, or surfaces that come into contact with prepared food or drink which in normal circumstances would be consumed without cooking. Those surfaces can include food mixing or washing vessels, 30 transport equipment such as conveyors, and filling and packaging equipment. Compositions for use in these industries generally contain or are diluted in uses to peracid concentrations of below 500 mg/l with corresponding concentrations of the other constituents. Such diluted compositions in practice are rarely 35 non-equilibrium in that over a period of time there would be a tendency for the peracid to re-equilibrate to hydrogen peroxide and carboxylic acid, but that is acceptable under disinfection treatment times. The use of the two component composition enables the process to be effected often without any pH alteration.

and the use of the three component composition is especially desirable in that it combines the advantage of the two component combination with that of a wider spectrum activity, even at approximately neutral or alkaline pH.

Having described the invention in general terms, specific embodiments 5 thereof will be described hereinafter in greater detail by way of non-limiting example only.

Comparisons CA to CD and Examples 1 and 2

In Comparison CA, the treatment employed was a dilutable grade of peracetic acid commercially available from Solvay Interox Limited under the 10 Trade Mark PROXITANE, containing 5% peracetic acid, 10% w/w acetic acid and 20% w/w hydrogen peroxide, diluted to give an in use concentration of peracid of 50 mg/l for the bacteria, and 200 mg/l for the yeast.

In Comparison CB, the treatment employed comprised 0.2% w/v active 15 ingredient of a quaternary ammonium cationic surfactant (QACS) available from Albright and Wilson under their Trade Mark EMPIGEN grade CM.

In Comparison CC, the composition employed comprised a solution of 10% w/v of an ethoxylated/propoxylated linear primary alcohol (alkoxylated alcohol) available from Union Carbide under their Trade Mark TRITON grade DF16.

In Comparison CD, the treatment employed was as in Comparison CA, 20 except that 0.2% w/v active ingredient of the QACS of Comparison CB was also employed.

In Example 1, the treatment employed was as for Comparison CA, except that 10% w/v of the (alkoxylated alcohol) of Comparison CC was also employed.

25 In Example 2, the treatment employed was as for Example 1, except that 0.2% w/v active ingredient of the QACS of Comparison CB was also employed.

The effectiveness of each of the various Comparison and Example 30 compositions as a microbicide was determined against three microbes considered to be representative for beverage industries, namely a yeast, Candida albicans, a gram negative bacterium, Pseudomonas aeruginosa, and a Gram-positive bacterium, Staphylococcus aureus.

The effectiveness of the composition as a microbicide was tested in a 35 disinfectant suspension test. The microbicide was challenged with an inoculum of the microbe containing a measured concentration of between 1×10^8 to 3×10^8 cfu for bacteria and between 1×10^7 and 3×10^7 cfu for the yeast in the presence of yeast extract (0.4%) and standard hard water for a period of 5

minutes at ambient temperature. The composition was quenched in the standard manners for peracid and surfactants depending on which components are present and thereafter determining the number of viable micro-organisms by conventional plate culture techniques. The studies were conducted in 5 duplicate.

The number of surviving viable bacteria or yeasts per unit volume (cfu) was then compared with the number before the disinfection treatment began, and the result given is the fraction that had been killed, expressed a logarithm, base 10; the higher the resultant number, the more effective the disinfection.

10 The maximum for the yeast was 4.6, for the gram -ve bacterium was 6.3 and 5.9 for the Gram +ve bacterium.

The results of the disinfection studies are summarised in Table 1 below

Table 1

Trial	pH	Measured Log Reduction Factor for		
		Yeast	Gram -ve Bacteria	Gram +ve Bacteria
5 CA	4	4.5	6.3	5.9
	6	3.3	3.5	4.4
	8	1.8	2.3	1.7
	10	0.3	1.4	0.6
10 CB	4	0.4	3.8	5.9
	6	0.7	0	5.9
	8	3.4	0	5.9
	10	4.6	0	5.9
15 CC	4	0.5	1.9	1.8
	6	0.7	0	0.7
	8	0.6	0	0.9
	10	0.6	0	1.1
20 CD	4	4.6	6.3	5.9
	6	4.6	3.5	5.9
	8	4.6	2.3	5.9
	10	4.6	1.1	5.9
Ex 1	4	4.6	6.3	5.9
	6	4.1	6.3	5.9
	8	2.9	4.9	5.0
	10	0.6	1.9	1.9
25 Ex 2	4	3.1	6.3	5.9
	6	0.6	6.3	5.9
	8	4.6	6.3	5.9
	10	4.5	2.5	4.5

30 From Table 1, it can be seen in Comparison CA that the effectiveness of peracetic acid as a microbicide is very good at acidic pHs of the region of pH 4, but that its effectiveness diminishes as the pH of the solution containing the yeast or bacterium increases. A comparison of Comparisons CA with CB and CD shows that the QACS complements the peracetic acid in terms as the pH 35 varies through the range tested for the yeast, without demonstrating synergism, but that there is no complementary action for the bacteria.

A comparison of Comparisons CA, CC and Example 1 demonstrates that the combination of the alkoxylated alcohol and peracetic acid offers similar performance to that of peracetic acid alone, at the low pH, and at higher pHs of from pH6 to pH10 shows synergism especially for the Gram negative

5 bacteria which are resistant to QACS. Thus, Table 1 shows that the pH range in which peracids retain their effectiveness is visibly extended from about pH4 without the alkoxylated alcohol up as high as about pH8 with the alkoxylated alcohol. Table 1 also shows complementary results or synergistic results for the Gram positive bacteria and the yeast at the higher pHs.

10 From a comparison of Examples 1 and 2, it can be seen that the addition of the QACS is beneficial at the high end of the pH range, and particularly at about pH8, complementing the other components and producing a composition that is especially effective for all three of the test micro-organisms.

15 Storage Stability Trial
To 247.5g of a sample of peracetic acid commercially available from Solvay Interox Limited under the Trade Mark PROXITANE, containing 5% peracetic acid, 10% w/w acetic acid and 20% w/w hydrogen peroxide was added 0.11g of a quaternary ammonium cationic surfactant (QACS) available from Albright
20 and Wilson under their Trade Mark EMPIGEN grade CM and 2.39g of an ethoxylated/propoxylated linear primary alcohol (alkoxyated alcohol) available from Union Carbide under their Trade Mark TRITON grade DF16. After 160 days storage at ambient temperature (ca. 20 - 25°C), analysis of the sample showed that 95% of the peracetic acid was retained, indicating that the sample
25 had excellent storage stability.

Claims:-

1. Peracid compositions having microbicidal activity over a broad pH range, characterised in that they comprise an effective amount of a peracid and a nonionic surfactant according to the general chemical formula (1):
$$R-(OCH_2CH_2)_n-(OCH_2CH_2CH_3)_p-O-R'$$
wherein R represents an alkyl group of at least 6 carbon atoms n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms.
2. A process for disinfection which comprises employing in combination a peracid and a nonionic surfactant according to the general chemical formula (1):
$$R-(OCH_2CH_2)_n-(OCH_2CH_2CH_3)_p-O-R'$$
wherein R represents an alkyl group of at least 6 carbon atoms n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms.
3. A composition or process according to claim 1 or 2 characterised in that the nonionic surfactant and peracid are present in a weight ratio selected within the range of from 10: 1 to 1 : 5, and preferably from 4 : 1 to 1 : 1.
4. A composition according to either preceding claim characterised in that the composition contains from about 1 to about 6% w/w peracid.
5. A composition according to any preceding claim characterised in that the peracid is peracetic acid.
6. A composition according to any preceding claim characterised in that it contains up to 0.5% w/w of a quaternary ammonium cationic surfactant.
7. A process for disinfection employing a composition as described in any preceding claim, either without or without dilution.
8. A process according to any of claims 2 to 7 characterised in that it is carried out at a pH of at least 6 and preferably from pH 6 to 8.

9. A process for preparing a composition according to any one of claims 1 or claims 3 to 6, characterised in that it comprises mixing a first solution comprising a peracid, with a second solution comprising a nonionic surfactant according to the general chemical formula (1):



wherein R represents an alkyl group of at least 6 carbon atoms n and p each represent an integer, and R' represents a short alkyl group of less than 6 carbon atoms.

10. A process or composition substantially as described herein with respect to any novel feature or novel combination of features.

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/GB 93/02520

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A01N37/16 // (A01N37/16, 25:30)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	DE,A,41 28 672 (HENKEL KGAA) 4 March 1993 see page 2, line 38 - page 2, line 54 see page 3, line 7 - page 3, line 26; claims; examples ---	1
A	EP,A,0 193 416 (L'AIR LIQUIDE) 3 September 1986 ---	
A	EP,A,0 397 217 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN) 14 November 1990 ---	
A	WO,A,88 00795 (F.GARCIN) 11 February 1988 ---	
A	US,A,4 240 921 (T.J.KANIECKI) 23 December 1980 -----	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- 'A' document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international filing date
- 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- 'O' document referring to an oral disclosure, use, exhibition or other means
- 'P' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

'&' document member of the same patent family

1 Date of the actual completion of the international search

Date of mailing of the international search report

7 March 1994

16.03.94

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl.
Fax (+ 31-70) 340-3016

Authorized officer

Donovan, T

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 93/02520

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE-A-4128672	04-03-93	WO-A-	9305135	18-03-93
EP-A-0193416	03-09-86	FR-A- AU-B- AU-A- CA-A- DE-A- JP-A- US-A-	2578332 579000 5266286 1292167 3661395 61217167 4743447	05-09-86 10-11-88 14-08-86 19-11-91 19-01-89 26-09-86 10-05-88
EP-A-0397217	14-11-90	DE-A- DE-A- EP-A, B EP-A- EP-A- EP-A- JP-A-	3636541 3779865 0265825 0397218 0397219 0397220 63122609	28-04-88 23-07-92 04-05-88 14-11-90 14-11-90 14-11-90 26-05-88
WO-A-8800795	11-02-88	FR-A- DE-A- EP-A, B	2601850 3781885 0280697	29-01-88 29-10-92 07-09-88
US-A-4240921	23-12-80	NONE		